

**O'Bryen, Barbara**

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**From:** Zara, Jane  
**Sent:** Thursday, December 27, 2001 12:07 PM  
**To:** O'Bryen, Barbara  
**Subject:** search request for 09/486,757

11D03

please search seq id No: 10, size unlimited search and oligo search. Thanks.

POINT OF CONTACT:  
BARB O'BRYEN  
TECH. INFORMATION SPECIALIST  
STIC CM1 ~~12014~~ 308-4291  
12E18

12013  
12-28-01

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| Set | Items | Description                                       |
|-----|-------|---------------------------------------------------|
| S1  | 29    | ALKALOID AND (CYTOCHROME (W) P450 (W) REDUCTASE?) |
| S2  | 13    | RD (unique items)                                 |

>>>KWIC option is not available in file(s): 41, 77, 399

2/3,K/1 (Item 1 from file: 5)  
 DIALOG(R)File 5:Biosis Previews(R)  
 (c) 2001 BIOSIS. All rts. reserv.

12606811 BIOSIS NO.: 200000360313  
**Induction of cytochrome P450 enzymes in the livers of rats treated with the pyrrolizidine \*alkaloid\* retrorsine.**  
 AUTHOR: Gordon Gavin J; Coleman William B(a); Grisham Joe W  
 AUTHOR ADDRESS: (a)Department of Pathology and Laboratory Medicine,  
 University of North Carolina School of Medicine, Chapel Hill, NC, 27599\*\*  
 USA  
 JOURNAL: Experimental and Molecular Pathology 69 (1):p17-26 August, 2000  
 MEDIUM: print  
 ISSN: 0014-4800  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

**Induction of cytochrome P450 enzymes in the livers of rats treated with the pyrrolizidine \*alkaloid\* retrorsine.**

ABSTRACT: Retrorsine is a member of the pyrrolizidine \*alkaloid\* (PA) family of naturally occurring compounds found in a large number of plant species worldwide. The cytotoxic, mutagenic, and antimitotic effects of PAs have made...

...REGISTRY NUMBERS: \*CYTOCHROME\* \*P450\* \*REDUCTASE\*;

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: ...CYP reductase {\*cytochrome\* \*P450\* \*reductase\*}; ...

...pyrrolizidine \*alkaloid\*--...

...metabolism, pyrrolizidine \*alkaloid\*, toxicity

2/3,K/2 (Item 2 from file: 5)  
 DIALOG(R)File 5:Biosis Previews(R)  
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11302695 BIOSIS NO.: 199800084027  
**Cloning and heterologous expression of NADPH-\*cytochrome\* \*P450\* \*reductase\* from the Papaveraceae.**  
 AUTHOR: Rosco Angela; Pauli Hubert H; Priesner Wiebke; Kutchan Toni M(a)  
 AUTHOR ADDRESS: (a)Lab. fuer Molekulare Biologie, Univ. Muenchen,  
 Karlstrasse 29, 80333 Muenchen\*\*Germany  
 JOURNAL: Archives of Biochemistry and Biophysics 348 (2):p369-377 Dec. 15, 1997

ISSN: 0003-9861  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**Cloning and heterologous expression of NADPH-\*cytochrome\* \*P450\*  
\*reductase\* from the Papaveraceae.**

ABSTRACT: \*Cytochrome\* \*P450\* \*reductase\* was purified to homogeneity from cell suspension cultures of the opium poppy *Papaver somniferum*, the enzyme was characterized (Km cytochrome c, 8.3  $\mu$ M; Km...

...California poppy) were then generated using the polymerase chain reaction and were used as hybridization probes to isolate full-length cDNAs. The *Papaver* and *Eschscholzia* \*cytochrome\* \*P450\* \*reductases\* are 63% identical at the nucleotide level and 69% identical at the amino acid level. SDS-PAGE of the purified native *P. somniferum* enzyme as well as genomic DNA gel blot analysis indicate that two \*cytochrome\* \*P450\* \*reductase\* isoforms are present in each species. This evidence is also supported by translation of nucleotide sequences obtained from the PCR-generated partial cDNAs and the full-length cDNAs isolated from lambda libraries. The *Papaver* and *Eschscholzia* \*cytochrome\* \*P450\* \*reductases\* were functionally expressed in the yeast *Saccharomyces cerevisiae* and in the insect cell culture *Spodoptera frugiperda* Sf9. Coexpression of \*cytochrome\* \*P450\* \*reductase\* with the C-O phenol coupling cytochrome P450 of bisbenzylisoquinoline \*alkaloid\* biosynthesis in *Berberis stolonifera*, berbaminine synthase (CYP80A1), in insect cell culture resulted in an alteration of the product profile as compared to that obtained by...

...REGISTRY NUMBERS: NADPH-\*CYTOCHROME\* \*P450\* \*REDUCTASE\*

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: NADPH-\*cytochrome\* \*P450\* \*reductase\*--

2/3,K/3 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2001 BIOSIS. All rts. reserv.

10064985 BIOSIS NO.: 199598519903

**Complete reversal by thaliblastine of 490-fold adriamycin resistance in multidrug-resistant (MDR) human breast cancer cells. Evidence that multiple biochemical changes in MDR cells need not correspond to multiple functional determinants for drug resistance.**

AUTHOR: Chen Guan; Waxman David J(a)

AUTHOR ADDRESS: (a)Div. Cell Molecular Biol., Dep. Biol., Boston Univ., 5  
Cummington St., Boston, MA 02215\*\*USA

JOURNAL: Journal of Pharmacology and Experimental Therapeutics 274 (3):p  
1271-1277 1995

ISSN: 0022-3565

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: as selective, potent and nontoxic modulators of drug resistance is thus an important goal for improving the success of cancer treatment. Thaliblastine (TBL), a plant \*alkaloid\* and P-glycoprotein (P-gp) inhibitor, is presently shown to fully reverse 490-fold resistance to Adriamycin (AdR) in a multidrug-resistant (MDR) human breast...

...REGISTRY NUMBERS: \*CYTOCHROME\* \*P450\* \*REDUCTASE\*

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: ...\*CYTOCHROME\* \*P450\* \*REDUCTASE\*

MISCELLANEOUS TERMS: ...\*CYTOCHROME\* \*P450\* \*REDUCTASE\*; ...

...PLANT \*ALKALOID\*;

2/3,K/4 (Item 4 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2001 BIOSIS. All rts. reserv.

09769773 BIOSIS NO.: 199598224691

**Molecular cloning and heterologous expression of a cDNA encoding  
berbamunine synthase, a C-O phenol-coupling cytochrome P450 from the  
higher plant *Berberis stolonifera*.**

AUTHOR: Kraus Peter F X; Kutchan Toni M(a)

AUTHOR ADDRESS: (a)Lab. Mol. Biol., Univ. Muenchen, Karlstrasse 29, 80333  
Munich\*\*Germany

JOURNAL: Proceedings of the National Academy of Sciences of the United  
States of America 92 (6):p2071-2075 1995

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: This cytochrome P450-dependent enzyme is unusual in that it catalyzes the regio- and stereoselective formation of a C-O phenol couple in bisbenzylisoquinoline \*alkaloid\* biosynthesis without concomitant incorporation of activated oxygen into the product. Consistent with the function of an oxidase rather than a monooxygenase, an essential glycine residue...  
...the equivalent position in berbaminine synthase. This oxidase was accumulated in an active form in insect cell microsomes and accepted electrons from the endogenous NADPH-\*cytochrome\* \*P450\* \*reductase\*. The heterologously expressed enzyme oxidatively couples either two molecules of (R)-N-methylcoclaurine to form the (R,R) dimer guatte-gaumerine or one molecule each...

2/3,K/5 (Item 5 from file: 5)

DIALOG(R)File 5: Biosis Previews(R)

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08753121 BIOSIS NO.: 199395042472

**Inhibition of rat liver microsomal lipid peroxidation by boldine.**

AUTHOR: Cederbaum Arthur I(a); Kukielka Ewa; Speisky Hernan

AUTHOR ADDRESS: (a)Dep. Biochemistry, Mount Sinai Sch. Med., One Gustave L.  
Levy Pl., New York, N.Y. 10029\*\*USA

JOURNAL: Biochemical Pharmacology 44 (9):p1765-1772 1992

ISSN: 0006-2952

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The \*alkaloid\* boldine, found in the leaves and bark of boldo, was an effective inhibitor of rat liver microsomal lipid peroxidation under a variety of conditions. The...

...produced nearly total inhibition of lipid peroxidation had no effect on microsomal mixed-function oxidase activity nor did boldine appear to direct electrons from NADPH-\*cytochrome\* \*P450\* \*reductase\* away from cytochrome P450. Boldine completely protected microsomal mixed-function oxidase activity against inactivation produced by lipid peroxidation. The effectiveness of boldine as an anti-oxidant under various conditions, and its low toxicity, suggest that this \*alkaloid\* may be an attractive agent for further evaluation as a clinically useful anti-oxidant.

2/3,K/6 (Item 1 from file: 73)

DIALOG(R)File 73: EMBASE

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07209686 EMBASE No: 1998104611

**Inhibition of cytochrome P450-dependent monooxygenases by an \*alkaloid\* fraction from *Helietta apiculata* markedly potentiates the hypnotic action of pentobarbital**

Goloubkova T.D.; Heckler E.; Rates S.M.K.; Henriques J.A.P.; Henriques

A.T.

A.T. Henriques, Graduate Course Pharmaceutical Sci., School of Pharmacy,  
UFRGS, Av. Ipiranga 2752, Porto Alegre, 90610-000 RS Brazil  
Journal of Ethnopharmacology ( J. ETHNOPHARMACOL. ) (Ireland) 1998, 60/2  
(141-148)  
CODEN: JOETD ISSN: 0378-8741  
PUBLISHER ITEM IDENTIFIER: S0378874197001396  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 20

**Inhibition of cytochrome P450-dependent monooxygenases by an \*alkaloid\* fraction from *Helietta apiculata* markedly potentiate the hypnotic action of pentobarbital**

Crude \*alkaloid\* fraction (CAF) isolated from the leaves of *Helietta apiculata* showed the presence of furoquinolines. The extract was investigated to determine if it can enhance the...

...i.p.) was associated with a statistically significant decrease of sleep latency and prolongation of pentobarbital-induced sleeping time. Pretreatment of rats with the same \*alkaloid\* extract (150 mg/kg, i.p. for 4 days) prior to administration of pentobarbital (40 mg/kg, i.p.) caused not only significant reduction of...

**DRUG DESCRIPTORS:**

\*\*cytochrome\* \*p450\* \*reductase\*--endogenous compound--ec; \*unspecific monooxygenase--endogenous compound--ec; \*medicinal plant--drug development--dv; \*medicinal plant--drug interaction--it; \*medicinal plant--pharmacology--pd; \*hypnotic agent--drug...  
...CAS REGISTRY NO.: 9075-42-7 (\*cytochrome\* \*p450\* \*reductase\*); 9012-80-0  
...

2/3,K/7 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

(c) 2001 Elsevier Science B.V. All rts. reserv.

07093772 EMBASE No: 1997375636

**A promoter region that controls basal and elicitor-inducible expression levels of the NADPH:\*cytochrome\* \*P450\* \*reductase\* gene (Cpr) from *Catharanthus roseus* binds nuclear factor GT-1**

Lopes Cardoso M.I.; Meijer A.H.; Rueb S.; Queiroz Machado J.; Memelink J.; Hoge J.H.C.

A.H. Meijer, Institute Molecular Plant Sciences, Leiden University, Clusius Laboratory, PO Box 9505, 2300 RA Leiden Netherlands

AUTHOR EMAIL: MEIJER@RULBIM.LEIDENUNIV.NL

Molecular and General Genetics ( MOL. GEN. GENET. ) (Germany) 1997, 256/6 (674-681)

CODEN: MGGEA ISSN: 0026-8925

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 38

**A promoter region that controls basal and elicitor-inducible expression levels of the NADPH:\*cytochrome\* \*P450\* \*reductase\* gene (Cpr) from *Catharanthus roseus* binds nuclear factor GT-1**

NADPH:\*cytochrome\* \*P450\* \*reductase\* (CPR) is essential for the activation of cytochrome P450 enzymes, which are involved in a wide variety of metabolic pathways in plants, including those related...

**DRUG DESCRIPTORS:**

indole \*alkaloid\*--endogenous compound--ec; messenger rna--endogenous compound--ec; terpenoid--endogenous compound--ec

2/3,K/8 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE

(c) 2001 Elsevier Science B.V. All rts. reserv.

06874374 EMBASE No: 1997158702

**The two faces of pyrrolizidine alkaloids: The role of the tertiary amine and its N-oxide in chemical defense of insects with acquired plant alkaloids**

Lindigkeit R.; Biller A.; Buch M.; Schiebel H.-M.; Boppre M.; Hartmann T.  
T. Hartmann, IPBTU, Mendelssohnstrasse 1, D-38106 Braunschweig Germany  
European Journal of Biochemistry ( EUR. J. BIOCHEM. ) (Germany) 1997,  
245/3 (626-636)  
CODEN: EJBCA ISSN: 0014-2956  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 55

...shows an almost complete loss of sup 1sup 80 label, indicating reduction of the orally fed N-oxide in the guts, uptake of the tertiary \*alkaloid\* and its reN-oxidation in the haemolymph. The enzyme responsible for N-oxidation is a soluble mixed function monooxygenase. It was isolated from the haemolymph...

...hydrophilic nontoxic N-oxide are discussed in respect to their bioactivation and detoxification in mammals and their role as defensive chemicals in specialized insects. Pyrrolizidine-\*alkaloid\*- sequestering insects store the alkaloids as nontoxic N-oxides which are reduced in the guts of any potential insectivore. The lipophilic tertiary \*alkaloid\* is absorbed passively and then bioactivated by cytochrome P-450 oxidase.

**DRUG DESCRIPTORS:**

\*pyrrolizidine \*alkaloid\*

\*cytochrome\* \*p450\* \*reductase\*; oxygenase

...CAS REGISTRY NO.: 9075-42-7 (\*cytochrome\* \*p450\* \*reductase\*); 9037-29-0

...

**2/3,K/9 (Item 1 from file: 94)**

DIALOG(R)File 94:JICST-EPlus

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04670506 JICST ACCESSION NUMBER: 00A0603727 FILE SEGMENT: JICST-E

**Intestinal Cytochrome P450 and Response to Rifampicin in Rabbits.**

NAKAMURA T (1); OKADA K (1); NAGATA K (1); YAMAZOE Y (1)

(1) Tohoku Univ., Sendai, Jpn

Jpn J Pharmacol, 2000, VOL.82,NO.3, PAGE.232-239, FIG.4, TBL.2, REF.32

JOURNAL NUMBER: G0813AAC ISSN NO: 0021-5198 CODEN: JJPAA

UNIVERSAL DECIMAL CLASSIFICATION: 615.45.033 615.33.015.1

LANGUAGE: English COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Journal

ARTICLE TYPE: Original paper

MEDIA TYPE: Printed Publication

...ABSTRACT: to assess the possibility of an experimental model for human intestinal oxidation of drugs. Significant amounts of P450 and cytochrome b5 and activities of NADPH-\*cytochrome\* \*P450\* \*reductase\* were detected in microsomes from rabbit duodenal, jejunal, ileac and colon mucosa. All the small intestinal fractions mediated phenytoin, dextromethorphan and testosterone oxidations. Several P450...

...DESCRIPTORS: morphinan \*alkaloid\*;

...BROADER DESCRIPTORS: \*alkaloid\*;

**2/3,K/10 (Item 2 from file: 94)**

DIALOG(R)File 94:JICST-EPlus

(c)2001 Japan Science and Tech Corp(JST). All rts. reserv.

04110689 JICST ACCESSION NUMBER: 99A0323992 FILE SEGMENT: JICST-E

**Examination on drug interaction of calcium antagonist nicardipine.**

NAKAMURA KATSUNORI (1); ARIYOSHI NORITAKA (1); YOKOI TSUYOSHI (1); KAMATAKI

TETSUYA (1); IWATSUBO TAKASHI (2); FUKUNAGA YASUHISA (2); HIGUCHI

SABURO (2); SHIMADA NORIAKI (3)

(1) Hokkaido Univ., Grad. Sch.; (2) Yamanouchi Pharm. Co., Ltd.; (3)  
Daiichi Pure Chem. Co., Ltd.  
Rinsho Yakuri (Japanese Journal of Clinical Pharmacology and Therapeutics),  
1999, VOL.30, NO.1, PAGE.85-86, FIG.1, TBL.1, REF.3  
JOURNAL NUMBER: F0384BAT ISSN NO: 0388-1601  
UNIVERSAL DECIMAL CLASSIFICATION: 615.2.015.2 615.45.033 615.225  
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan  
DOCUMENT TYPE: Journal  
ARTICLE TYPE: Original paper  
MEDIA TYPE: Printed Publication

...DESCRIPTORS: morphinan \*alkaloid\*;  
...IDENTIFIERS: NADPH \*cytochrome\* \*P450\* \*reductase\*  
...BROADER DESCRIPTORS: \*alkaloid\*;

2/3,K/11 (Item 1 from file: 315)  
DIALOG(R) File 315: ChemEng & Biotech Abs  
(c) 2001 DECHEMA. All rts. reserv.

463867 CEABA Accession No.: 30-08-013330 DOCUMENT TYPE: Patent  
**Title: \*Cytochrome\* \*P450\* \*reductases\* from poppy plants.**  
AUTHOR: Kutchan, T. M. ; Atkins, D. G. ; Fist, A. J.  
CORPORATE SOURCE: Johnson & Johnson Res. Pty Ltd. Rushcutters Bay, NSW 2011  
Australia  
CODEN: PIXXD2  
PATENT NUMBER: WO 9911765  
PUBLICATION DATE: 11 Mar 1999 (19990311) LANGUAGE: English  
PRIORITY PATENT APPLICATION(S) & DATE(S): AU 8872 (19970829)

**Title: \*Cytochrome\* \*P450\* \*reductases\* from poppy plants.**

...ABSTRACT: is disclosed for the production of alkaloids from poppy plants and in particular to a gene encoding the cytochrome P-450 reductase enzyme in the \*alkaloid\* pathway. Also disclosed are proteins encoded by the gene, plants transformed or transfected with the gene, and methods for altering the \*alkaloid\* content or blend of poppy plants. ...

DESCRIPTORS: English ; \*alkaloid\* ; cytochrome P-450 ; transgenic plant ; genetic manipulation ; plant breeding ; pharmaceutical production ; reducing enzymes

2/3,K/12 (Item 1 from file: 357)  
DIALOG(R) File 357: Derwent Biotechnology Abs  
(c) 2001 Derwent Publ Ltd. All rts. reserv.

0236841 DBA Accession No.: 99-06942 PATENT  
**Nucleic acid encoding \*cytochrome\*-\*P450\*-\*reductase\* from poppy -  
transgenic plant construction with increased yield of morphine,  
codeine, thebain or oripavine**  
AUTHOR: Kutchan T M; Zenk M H; Atkins D G; Fist A J  
CORPORATE SOURCE: Rushcutters Bay, NSW, Australia.  
PATENT ASSIGNEE: Johnson+Johnson 1999  
PATENT NUMBER: WO 9911765 PATENT DATE: 990311 WPI ACCESSION NO.:  
99-214703 (9918)  
PRIORITY APPLIC. NO.: AU 978872 APPLIC. DATE: 970829  
NATIONAL APPLIC. NO.: WO 98AU705 APPLIC. DATE: 980828  
LANGUAGE: English

**Nucleic acid encoding \*cytochrome\*-\*P450\*-\*reductase\* from poppy**

ABSTRACT: Isolated, purified nucleic acid (I) encoding \*cytochrome\*-\*P450\*-\*reductase\* (II) from an \*alkaloid\* poppy is claimed. Also claimed are: eukaryotic or prokaryotic expression of (II) in at least 1 of the extracellular environment or intracellular membrane or cytoplasmic...

... expressing (I) or the constructs; cells, callus or transgenic plants produced by transfection or transformation with (I) or the constructs; a crop of stably reproducing \*alkaloid\* producing poppies transformed



or transfected with (I) of the constructs, their straw and straw concentrate; alkaloids (III) from the straw of the poppies; and production of (III) from the transgenic plants. The \*alkaloid\* is an analgesic. Transformation of the plants with (I) alters the yield and/or type of (III) produced, especially it increases the yield of (III)...

DESCRIPTORS: poppy transgenic plant construction, \*cytochrome\*-P450\*-reductase\* gene expression, DNA construct, DNA probe, DNA primer, sense, antisense DNA, vector, transformed cell, callus culture, pot. crop improvement, increased \*alkaloid\* e.g. morphine, codeine, oripavine, thebaine content cell culture medicinal plant gene transfer hybridization enzyme analgesic narcotic sedative arene cycloalkane het-N het-O ring...

2/3,K/13 (Item 1 from file: 399)  
DIALOG(R) File 399:CA SEARCH(R)  
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130206693 CA: 130(16)206693q PATENT  
Cloning and heterologous expression of NADPH-cytochrome P 450 reductases from poppy plants  
INVENTOR(AUTHOR): Kutchan, Toni Mary; Zenk, Meinhart Hans; Atkins, David George; Fist, Anthony John  
LOCATION: Australia  
ASSIGNEE: Johnson & Johnson Research Pty. Limited  
PATENT: PCT International ; WO 9911765 A1 DATE: 19990311  
APPLICATION: WO 98AU705 (19980828) \*AU 978872 (19970829)  
PAGES: 58 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-009/02A;  
C12N-015/53B DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; HR; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH ; GM; KE; LS; MW; SD; SZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG  
?